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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/539,486	03/30/2000	SERGEY A. SELIFONOV	02-028940US	8406

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EXAMINER

ZHOU, SHUBO

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 06/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/539,486

Applicant(s)

SELIFONOV ET AL.

Examiner

Shubo (Joe) Zhou

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 March 2005.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-8,10-24,26-29,31-46,99 and 100 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1,3-8,10-24,26-29,31-46,99 and 100 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
10) ☒ The drawing(s) filed on 01 June 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 3/28/05.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment and request for reconsideration in the communication filed on 3/28/05 is acknowledged and the amendment entered.

Claims 1, 3-8, 10-24, 26-29, 31-46 and 99-100 are currently pending and under examination.

Applicant's arguments in response to the previous Office action have been fully considered. The following rejections and/or objections are either reiterated from the previous Office action, mailed 1/3/05, or newly added, and constitute the complete set presently being applied to the instant application. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

The rejections of claims 1-24, 25-29, 31-46 and 99-100 under 35 USC 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is hereby withdrawn in view of applicants' amendment to the claims.

The rejection of claims 1-24, 26-29, 31-46 and 99-100 provisionally under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 99-101, 105-112 of US copending Application No. 09/494,282 is hereby withdrawn in view of the terminal disclaimer filed 3/28/05.

Declaration

The objection in the previous Office action to the declaration filed 7/13/2000 is hereby withdrawn in view of applicants' argument (page 17).

Information Disclosure Statements

The Information Disclosure Statements filed on 3/28/05 is entered and the reference therein has been considered. A signed copy of the PTO-1449 is herein attached.

Specification

The specification is objected to because of the following:

The disclosure is objected to because it contains an embedded hyperlink and/or other form or browser-executable code. Such code is present in the specification on 9 and other pages. Applicants are required to delete the embedded hyperlink and/or other form of browser-executable code on this page and such codes anywhere else in the specification. See MPEP ' 608.01.

This rejection is reiterated from the previous Office action and maintained for reasons of record. Applicants amended the specification to only remove the "http://" for the browser-executable codes present in the specification, e.g. the "<http://www.ncbi.nlm.nih.gov>" on page 16. However, those hyperlink without <http://> are still browser-executable. The phrase "www." needs also be removed.

The phrase " to from" on page 87, line 22, appears to be a typographical error for "to form".

The phrase "Fig. 11 is a continuation of figure 13" on page 8, line 7, appears to be a typographical error for "Fig. 11 is a continuation of figure 10".

Appropriate correction is required.

Claim Rejections-35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-8, 10-24, 26-29, 31-46 and 99-100 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The meaning of the phrase "which character strings, when aligned for maximum identity, comprise at least one region of heterology" in independent claims 1 and 39, as well as their respective dependent claims, is unclear. It is not clear whether the sequence in the "region of heterology" is different in each and every one of the plurality of parental character strings or only in some thereof.

The meaning of the phrase "providing a set of oligonucleotides corresponding to the set of character string subsequences" in independent claims 1 and 39, as well as their respective dependent claims, is unclear due to the use of the phrase "corresponding to." It is not clear whether the oligonucleotides provided correspond to the subsequences by having the same sequences thereof, or by having sequences complementary to the subsequences.

The meaning of the phrase "wherein the subsequences from each parental character string are separated by a crossover point" in independent claims 1 and 39, as well as their respective dependent claims, is unclear. Firstly, the phrase "the subsequences from each parental character

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string” in line 19 of claim 1 lacks clear antecedent basis. Secondly, it is not clear whether “the subsequences” recited in line 19 of claim 1 are only those same subsequences recited in line 9 of the claim, to which the set of oligonucleotides provided in line 8 are corresponded, or they also include the “subsequence from each of at least two parental character strings”, which subsequence is comprised in the chimeric nucleic acid sequence” recited in line 17 of claim 1. Thirdly, it is not clear whether the crossover point is within a subsequence represented by an oligonucleotide that comprises a chimeric sequence comprising a subsequence from each of at least two parental character strings, as recited in lines 16-18, or the crossover point is between two subsequences, each of which is represented by an oligonucleotide provided.

The meaning of the phrase “wherein at least one crossover point for at least one oligonucleotide member is selected from a region outside of an identified pairwise homology region” recited in independent claims 1 and 39, as well as their respective dependent claims, is unclear. It is not clear whether the crossover point is outside of all pairwise regions of all the parental character strings, or it is just outside of “an pairwise region” because “a region outside of an identified pairwise homology region” of two parental strings could well be inside of a pairwise homology region of two other parental strings.

The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-8, 10-24, 26-29, 31-46 and 99-100 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling annealing members of a set of

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oligonucleotides corresponding to a set of character string subsequences, wherein each of the oligonucleotides is complementary to at least one other oligonucleotide of the set, does not reasonably provide enablement for annealing members of the set of oligonucleotides wherein none of the oligonucleotides is complementary to at least one other oligonucleotide.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)), the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation; (b) the amount of guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the predictability of the prior art; (g) the breadth of the claims; and (h) the relative skill in the art. The factors are analyzed for the instant case as follows:

(a) In the instant case, the amount of experimentation required by the skilled artisan in order to practice of making the claimed polypeptides would require an unpredictable amount of experimentation for the following reasons:

(b) The claims require annealing among members of a set of oligonucleotides, which are provided corresponding to a set of subsequences. However, the steps of the method in the claims, e.g. claim 1, prior to the annealing step do not set forth any complementarity between members of the set of oligonucleotides. As set forth in the rejection under 35 USC 112, second paragraph above, due to the use of the phrase "corresponding to", at least some of the oligonucleotides provides are not complementary between one and another. There is no guidance in the instant specification that teaches the skilled artisan how to anneal oligonucleotides that are not complementary from one another.

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(c) The instant application does not present any working examples wherein oligonucleotides that are not complementary from one another are annealed.

(d)-(f) The nature of the invention, annealing of nucleic acids that are not complementary from one another, is complex. The prior art teaches how nucleic acids that are complementary from one another are annealed. For example, Darnell et al. (page 237, Molecular Cell Biology, Scientific American Books, 1986) states:

Under the conditions of temperature and ion concentration found in cells, DNA is maintained as a duplex (two-stranded) structure by the many hydrogen bonds of the A-T and G-C base pairs. The two strands of the duplexes can be melted (separated) by heating them (usually in a dilute salt solution – e.g., 0.01 M NaCl) or by raising the pH to higher than 11. If the temperature is then lowered and the concentration of ions in the solution is raised, or if the pH is lowered, the single strands will anneal, or reassociate, to reconstitute duplexes (provided that their concentration in the solution is high enough). Only complementary strands reassociate, and the extent of their reassociation is virtually unaffected by the presence of noncomplementary strands.

The prior art does not teach annealing of nucleic acids that are not complementary.

(g)-(h) As set forth above, the claims, which requires providing of oligonucleotides corresponding to a set of subsequences, are broad especially because the oligonucleotides provided can have various sequences due to the unclarity of the phrase “corresponding to.” The level of skill of those in the art who practice providing oligonucleotides corresponding to a set of subsequences and annealing of the oligonucleotides is high.

The skilled practitioner would first turn to the instant specification for guidance in practice of annealing nucleic acids that are not complementary. However, the specification does not provide sufficient guidance of practicing the same. As such, the skilled practitioner would turn to the prior art for such guidance. However, the prior art does not teach such a method. Finally, said practitioner would turn to trial and error experimentation for annealing nucleic acids that are not complementary without guidance from the specification or the prior art. Therefore, undue experimentation becomes the burden of the practitioner.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst Tina Plunkett whose phone number is (571) 272-0549.

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Shubo (Joe) Zhou, Ph.D.



Patent Examiner

 9 June 2005**JOHN S. BRUSCA, PH.D.
PRIMARY EXAMINER**